IN THE CLAIMS

Claims 1-18 are canceled without prejudice or disclaimer of the subject matter thereof.

Please add new claims 19-38 as follows:

19. (New) A method for generating an antagonist of the pro-survival Bcl-2 family, said method comprising;

selecting a scaffold BH3-only protein structure with residue positions defining an amphipathic α-helix formed by the BH3 domain;

selecting one or more residue positions associated with a promiscuous binding phenotype of a BH3-only protein;

substituting amino acid residues conferring a promiscuous phenotype for a molecule selected from the group consisting of amino acids and amino acid chemical analogs which confer a restrictive binding pattern to a Bcl-2 protein; and

analyzing the interaction of each substitution for an ability to induce a more restrictive spectrum of binding to a Bcl-2 protein.

20. (New) The method of Claim 19 wherein said Bcl-2 antagonist is specific for one or more molecules selected from the group consisting of Bcl-2, BCl-XL, Bcl-w, Mcl and Al.

21. (New) The method of Claim 19 wherein said Bcl-2 antagonist is based on the structure of a molecule selected from the group consisting of Noxa, Bim, Puma, Bmf, Bad, Bik, Hrk and Bid.

22. (New) The method of Claim 19 wherein said Bcl-2 antagonist inhibits a pro-survival protein on a cancer cell.

23. (New) The method of Claim 22 wherein said cancer cell is selected from the group consisting of ABL1 protooncogene, AIDS Related Cancers, Acoustic Neuroma,

Acute Lymphocytic Leukaemia, Acute Myeloid Leukaemia, Adenocystic carcinoma, Adrenocortical Cancer, Agnogenic myeloid metaplasia, Alopecia, Alveolar soft-part sarcoma, Anal cancer, Angiosarcoma, Aplastic Anaemia, Astrocytoma, Ataxia-telangiectasia, Basal Cell Carcinoma (Skin), Bladder Cancer, Bone Cancers, Bowel cancer, Brain Stem Glioma, Brain and CNS Tumors, Breast Cancer, CNS Tumors, Carcinoid Tumors, Cervical Cancer, Childhood Brain Tumors, Childhood Cancer, Childhood Leukaemia, Childhood Soft Tissue Sarcoma, Chondrosarcoma, Choriocarcinoma, Chronic Lymphocytic Leukaemia, Chronic Myeloid Leukaemia, Colorectal Cancers, Cutaneous T-Cell Lymphoma, Dermatofibrosarcoma-protuberans, Desmoplastic-Small-Round-Cell-Tumor, Ductal Carcinoma, Endocrine Cancers, Endometrial Cancer, Ependymoma, Esophageal Cancer, Ewing's Sarcoma, Extra-Hepatic Bile Duct Cancer, Eye Cancer, Eye: Melanoma, Retinoblastoma, Fallopian Tube cancer, Fanconi Anaemia, Fibrosarcoma, Gall Bladder Cancer, Gastric Cancer, Gastrointestinal Cancers, Gastrointestinal-Carcinoid-Tumor, Genitourinary Cancers, Germ Cell Tumors, Gestational-Trophoblastic-Disease, Glioma, Gynaecological Cancers, Haematological Malignancies, Hairy Cell Leukaemia, Head and Neck Cancer, Hepatocellular Cancer, Hereditary Breast Cancer, Histiocytosis, Hodgkin's Disease, Human Papillomavirus, Hydatidiform mole, Hypercalcemia, Hypopharynx Cancer, IntraOcular Melanoma, Islet cell cancer, Kapos's sarcoma, Kidney Cancer, Langerhan's-Cell-Histiocytosis, Laryngeal Cancer, Leiomyosarcoma, Leukaemia, Li- Fraumeni Syndrome, Lip Cancer, Liposarcoma, Liver Cancer, Lung Cancer, Lymphedema, Lymphoma, Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma, Male Breast Cancer, Malignant-Rhabdoid-Tumor-of-Kidney, Medulloblastoma, Melanoma, Merkel Cell Cancer, Mesothelioma, Metastatic Cancer, Mouth Cancer, Multiple Endocrine Neoplasia, Mycosis Fungoides, Myelodysplastic Syndromes, Myeloma, Myeloproliferative Disorders, Nasal Cancer, Nasopharyngeal Cancer, Nephroblastoma, Neuroblastoma, Neurofibromatosis, Nijmegen Breakage Syndrome, Non-Melanoma Skin Cancer, Non- Small-Cell-Lung-Cancer-(NSCLC), Ocular Cancers, Oesophageal Cancer, Oral cavity Cancer, Oropharynx Cancer, Osteosarcoma, Ostomy Ovarian Cancer, Pancreas Cancer, Paranasal Cancer, Parathyroid Cancer, Parotid Gland Cancer, Penile Cancer, Peripheral- Neuroectodermal-Tumors, Pituitary Cancer, Polycythemia vera, Prostate Cancer, Rare- cancers-and-associated-disorders, Renal Cell Carcinoma, Retinoblastoma, Rhabdomyosarcoma,

Rothmund-Thomson Syndrome, Salivary Gland Cancer, Sarcoma, Schwannoma, Sezary syndrome, Skin Cancer, Small Cell Lung Cancer (SCLC), Small Intestine Cancer, Soft Tissue Sarcoma, Spinal Cord Tumors, Squamous-Cell-Carcinoma- (skin), Stomach Cancer, Synovial sarcoma, Testicular Cancer, Thymus Cancer, Thyroid Cancer, Transitional-Cell-Cancer- (bladder), Transitional-Cell-Cancer- (renal-pelvis-/- ureter), Trophoblastic Cancer, Urethral Cancer, Urinary System Cancer, Uroplakins, Uterine sarcoma, Uterus Cancer, Vaginal Cancer, Vulva Cancer, Waldenstrom's-Macroglobulinemia, and Wilms'Tumor.

24. (New) The method of Claim 19 wherein said Bcl-2 antagonist inhibits a prosurvival protein in a mammal.

25. (New) The method of Claim 24, wherein said mammal is a human.

26. (New) A method for generating an antagonist of the pro-survival Bcl-2 protein family, said method comprising;

selecting a restrictive BH3-only protein as a scaffold protein;

determining the conformation of the scaffold conferring the restrictive phenotype; and

generating a chemical compound which mimics said scaffold and conformational part conferring a restrictive spectrum of binding to a Bcl-2 protein.

27. (New) A method for selecting an antagonist of the pro-survival Bcl-2 protein family, said method comprising;

selecting a restrictive BH3-only protein as a scaffold protein;

determining the conformation of the scaffold conferring the restrictive phenotype; and

generating a chemical compound which mimics said scaffold and conformational part conferring a restrictive spectrum of binding to a Bcl-2 protein.

28. (New) A computational method for designing an antagonist of the pro-survival Bcl-2 protein family based on a scaffold BH3-only protein with residue positions conferring a restrictive phenotype comprising;

selecting a collection of promiscuous BH3- only proteins;

providing a sequence alignment of said proteins and comparing said sequence alignment to a restrictive BH3-only protein;

generating a frequency of occurrence for individual amino acids in one or a plurality of positions with said alignments conferring promiscuity or restrictivity with respect to binding to Bcl-2 proteins;

creating a scoring function selected from the group consisting of charge, size, conformation, solubility, polarity, hydrophobicity, hydrophilicity and contribution to tertiary structure using said frequencies;

using said scoring function and at least one additional scoring function to generate information selected from the group consisting of a set of optimized protein sequences and the conformational equivalents of optimized protein sequences; and

performing an activity selected from the group consisting of generating a compound having a restrictive binding phenotype to a Bcl-2 protein and selecting a protein having a restrictive binding phenotype to a Bcl-2 protein.

29. (New) The method of Claim 28 wherein said scoring function is selected from the group consisting of the number and position of acidic residues, the number and position of basic residues, the number and position of polar residues, the number and position of non-polar residues, the number and position of charged residues, the number and position of uncharged residues, the number and position of hydrophilic residues, the number and position of hydrophobic residues, the levels of residues, the solubility levels of residues, the size of residues, and the contribution to tertiary structure the residue makes in the BH3-only protein.

30. (New) A computer program product for determining the structure of an agent to induce apoptosis in a cell, said product comprising:

(1) code that receives as input scoring function (SF) for at least two features associated with a molecule selected from the group consisting of BH3-only and Bcl-2, wherein said features are selected from the group consisting of: (m) the number and position of acidic residues, (n) the number and position of basic residues, (o) the number and position of polar residues, (p) the number and position of non-polar residues, (q) the number and position of charged residues, (r) the number and position of uncharged residues, (s) the number and position of hydrophillic residues, (t) the number and position of hydrophobic residues, (u) the levels of residues, (v) the solubility levels of residues, (w) the size of residues, and (x) the contribution to tertiary structure the residue makes in the BH3- only protein;

(2) code that adds said SF to provide a sum corresponding to a Pv for BH3-only proteins; and

(3) a computer readable medium that stores the codes.

31. (New) An apparatus for assessing the likely usefulness of a BH3-only protein or chemical equivalent to induce apoptosis in a cell comprising;

(1) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise lys for at least two features associated with a molecule selected from the group consisting of BH3-only and Bcl-2, wherein said features are selected from the group consisting of: (m) the number and position of acidic residues, (n) the number and position of basic residues, (o) the number and position of polar residues, (p) the number and position of non-polar residues, (q) the number and position of charged residues, (r) the number and position of uncharged residues, (s) the number and position of hydrophillic residues, (t) the number and position of hydrophobic residues, (u) the levels of residues, (v) the solubility levels of residues, (w) the size of residues, and (x) the contribution to tertiary structure the residue makes in the BH3- only protein;

(2) a working memory for storing instructions for processing said machine-readable data;

(3) a central-processing unit coupled to said working memory and to said machine-readable data storage medium, for processing said machine readable data to provide a sum of said SF corresponding to a Pv for said compound (s); and

(4) an output hardware coupled to said central processing unit, for receiving said Pv.

32. (New) A method of treating cancer in a subject comprising;

administering to said subject an effective amount of an antagonist of a Bcl-2 protein for a time and under conditions sufficient to decrease said cancer.

33. (New) The method of Claim 32, further comprising one or more pharmaceutically acceptable carriers or diluents.

34. (New) The method of Claim 32 wherein administration of said antagonist is accomplished by a method selected from the group consisting of respiratoral, intratracheal, nasopharyngeal, intravenous, intraperitoneal, subcutaneous, intracranial, intradermal, intramuscular, intraoccular, intrathecal, intracereberal, intranasal, infusion, oral, rectal, patch and implant rates.

35. (New) A method of preventing cancer in a subject comprising;

administering to said subject an effective amount of an antagonist of a Bcl-2 protein for a time and under conditions sufficient to prevent said cancer.

36. (New) The method of Claim 35 further comprising one or more pharmaceutically acceptable carriers or diluents.

37. (New) The method of Claim 35 wherein administration of said antagonist is accomplished by a method selected from the group consisting of respiratoral, intratracheal, nasopharyngeal, intravenous, intraperitoneal, subcutaneous, intracranial,